REMARKS

The document is submitted in reply to the Office Action dated August 20, 2009 ("Office Action"). Applicants have amended claims 6 and 40-45 to promote clarity. The wild type SPE-C polypeptide sequence (SEQ ID NO: 2) appears in the Specification at page 17, lines 16-20. Support for "an Y15A mutation" (claim 40) or "an Y15A mutation and an R181Q mutation" (claims 41) can be found in the Specification at page 15, lines 4-5. Support for the mutations recited in claim 42 appears in the Specification at page 17, line 21 to page 18, line 5. Support for "a deletion of residues of 22-90 of SEQ ID NO: 2" (claim 43) can be found in the Specification, at pages 19-20, carryover paragraph. Support for the amendments to claims 44 and 45 can be found in the Specification at page 15, lines 2-4. Applicants have also amended claims 15-17, 21, and 26 to correct informalities. No new matter is added.

Upon entry of the proposed amendments, claims 2-6, 10, 11, 13, 15-18, 21-26, 28-38, and 40-45 will be pending. Claims 17, 18, 21-26, and 28-38 have been withdrawn from consideration and claims 2-6, 10, 11, 13, 15, 16 and 40-45 are under examination. Applicants respectfully request that the Examiner reconsider this application in view of the following remarks.

35 U.S.C. § 112 Rejections

Claims 40-45 were rejected for indefiniteness. See the Office Action, page 2, item 5. According to the Examiner, "[t]he claims are indefinite in the recitation of specific amino acid residues of SPE-C in the absence of a SEQ ID NO." See page 2, last paragraph. In the sole interest of moving this case forward, Applicants have amended these claims to recite "SEQ ID NO: 2." In view of the amendments, Applicants submit that claims 40-45 as amended now are definite.

35 U.S.C. § 103 Rejections

The Examiner rejected claims 2-6, 10-11, 13, 15, 16, 40-41, and 44-45 for obviousness over WO95/31483 by Cardy *et al.* ("Cardy") in view of WO 98/24190 by

Schlievert *et al.* ("Schlievert"). See the Office Action, page 3, item 6. Applicants respectfully traverse and will discuss independent claim 2 first.

Claim 2 is drawn to a conjugate comprising two parts: (1) an antigen-presenting cell (APC) targeting molecule and (2) an antigen that is coupled to the APC targeting molecule. The APC-targeting molecule is a mutated superantigen having one or more mutations only in its T cell binding site as compared to its wild-type counterpart. The conjugate is capable of binding to a Class II MHC molecule. An example of the APC-targeting molecule is an SPE-C superantigen mutant.

Cardy, the primary reference, describes a polypeptide conjugate having two parts: (a) "a binding portion having specific binding affinity for a eukaryotic target cell surface component," such as MHC class II molecules, and (b) "an effector portion ... capable of exerting a biological effect." See Cardy, pages 2-3, carryover paragraph. According to the Office Action, Schlievert, the secondary reference, "teaches that superantigens such as SPE-C function to bind to MHC class II molecules." See the Office Action, page 4, lines 13-4. As such, the Examiner concluded that "it would have been *prima facie* obvious to one of ordinary skill in the art ... to use an MHC binding SPE-C superantigen as taught by [Schlievert], as the MHC targeting portion in the conjugate polypeptides taught by [Cardy]." See the Office Action, page 4, third paragraph. Applicants disagree.

First, Applicants would like to point out that the two cited references, alone or combined, do not suggest one of ordinary skill in the art to substitute the "binding portion" of the Cardy conjugate with a Schlievert superantigen in the manner asserted by the Examiner. More specifically, Cardy explicitly teaches that the "binding portion" must be one "having specific binding affinity" for a eukaryotic target cell surface component. See page 3, line 1, and claim 1. In other words, if an agent is unspecific for the surface component on the target cell, it is not within the scope of the binding portion. Indeed, to this end, Cardy provides a large number of examples for the binding portion. Markedly, all of them are antibodies. See, e.g., Examples 1-9. It was well known in the art that antibodies are used because of their high specificity. Thus, in view of the Cardy's focus on specific antibodies and extensive description of these antibodies, one of ordinary

skill in the art would have appreciated that the Cardy binding portion does not cover an agent that is not specific for a surface component on a particular target cell.

In this connection, Applicants note that, unlike those specific antibodies described in Cardy, the SPE-C superantigen in Schlievert has several, diverse binding activities. These includes "binding to porcine aortic endothelial cells," "binding to MHC class II molecules," and "binding to T-cell receptors." See Schlievert, page 7, third paragraph. In view of these diverse and various binding activities, one of ordinary skill in the art would have concluded, the Schlievert SPE-C superantigen, unlike the Cardy antibodies, is not specific for a surface component on a particular target cell, and therefore not suitable as a binding portion in the Cardy conjugate. It follows that he or she would not have been motivated to substitute the "binding portion" of the Cardy conjugate with a Schlievert superantigen in the manner asserted by the Examiner.

Second, Applicants note that the SPE-C superantigen in Schlievert and the antibodies in Cardy are structurally and functionally different. They have different biological functions and attributes. Antibodies are large mutli-chain proteins that possess bivalent antigen binding and also function as effector in innate immunity. Because of their bifunctional binding they have the unique ability to cross-link surface receptors creating an unwanted cell activation or cell death. In Cardy, bifunctional binding of antibody to its cell surface receptor is necessary for it to work at a suitable therapeutic dose. On the other hand, the Schlievert superantigen does not have the same effect and therefore one of ordinary skill in the art would not substitute the "binding portion" of the Cardy conjugate with a Schlievert superantigen in the manner asserted by the Examiner, much less a mutant superantigen as recited in claim 2.

For the above remarks, Applicants submit that the Examiner has not established a *prima facie* case of obviousness against claim 2. Even if a *prima facie* case of obviousness were established, which Applicants do not concede, it could be successfully rebutted by a showing of an unexpected property of the claimed conjugate as compared with the closest prior art conjugate, i.e., the Cardy conjugate.

As pointed out in the Specification, it was unexpected that a molecule which mimics a superantigen but which lacks a fully functional TcR binding site can, when coupled to an immunomodulatory antigen, bind and activate APCs to a degree not previously known or suspected. Due to this, immunomodulatory constructs are effective in antigen presentation without the requirement to bind to the TcR. This is of particular relevance to moieties which have low or nonexistent immunogenicity, such as peptides, proteins, nucleic acids, whole viruses etc. See the Specification, page 6, lines 11-17.[1]

In addition, the superantigen itself can elicit immune response which in turn increases the antigenicity of an antigen conjugated to it. See the Specification, page 6, lines 18-27.

The above-discussed properties were unexpected as they were not contemplated by Cardy, or Schlievert in that matter, at all. In contrast, in Cardy, the "binding portion" has only one function, i.e., to deliver an effector to a particular cell. See page 1, lines 6-12. In view of that, one of ordinary skill in the art would not have expected that the Cardy "binding portion" would enhance immune response. To the extent that the sole function of the Cardy "binding portion" is to deliver an effector to a particular cell, Cardy in effect teaches away one of ordinary skill in the art from using a superantigen as recited in claim 2. Further, the conjugate of claim 2 enjoys other advantages over the antibody-based Cardy conjugate. For example, while antibodies are unstable and difficulty to produce in large amounts, superantigens on the other hand are small compact, highly stable polypeptides which can be produced in large amounts.

In sum, the above-discussed unexpected properties of the conjugate of claim 2 rebut the obviousness rejection. Thus, Applicants submit that claim 2 is non-obvious over Cardy in view of Schlievert. So are claims 3-6, 10-11, 13, 15, 16, 40-41, and 44-45, all of which depend from claim 2 directly or indirectly.

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[1] Rebuttal evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, *In re Chu*, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995). See MPEP 2145.

Conclusion

It is believed that all of the pending claims have been addressed. However, the absence of a reply to a specific rejection, issue or comment does not signify agreement with or concession of that rejection, issue or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

The Petition for Extension of Time fee in the amount of $65 is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to Deposit Account No. 50-4189, referencing Attorney Docket No. 55503-002001.

Respectfully submitted,

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Jianming Hao, Ph.D.
Reg. No. 54,694

Customer No. 69713
Occhiuti Rohlicek & Tsao LLP
10 Fawcett Street
Cambridge, MA 02138
Telephone: (617) 500-2512
Facsimile: (617) 500-2499